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Cohort

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13. ABSTRACT (Maximum 200 Words) Ecologic studies implicate a "western" diet in prostate cancer, but whether dietary patterns measured in individuals are associated with risk has not been studied previously. We used prospective data from the NHANES I Epidemiologic Follow-up Study, with 136 cases among 3,779 men followed 1982-4 to 1992. Using principal components analysis, three patterns were identified: vegetable-fruit, red meat-starch, and southern. In proportional hazards models, southern pattern intake showed a risk reduction (3rd vs. 1st tertile RR 0.6, 95% CI 0.4-1.1) that approached statistical significance, was observed in black and non-black men, and was not attributable to intake of any individual foods or nutrients. A southern pattern may reflect a history of living in the South and serve as a marker of sunlight exposure and protection through 1,25-hydroxyvitamin D production. Other findings in the same sample also suggest the importance of a vitamin D-related pathway: Dairy intake (RR 2.2, 95% CI 1.3-4.0), lowfat milk (RR 1.6, 95% CI 1.2-2.1), and calcium (RR 2.4, 95% CI 1.5-3.9) were associated with risk, while vitamin D intake was inversely associated (RR 0.5, 95% CI 0.3-1.0). High calcium intake may suppress 1,25-hydroxyvitamin D production, increasing prostate cancer risk. However, mechanisms linking dairy/calcium to prostate cancer should be clarified and confirmed.				
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INTRODUCTION

While epidemiologic studies and intervention trials on diet and prostate cancer have focused primarily on specific factors in the diet, associations of dietary patterns with prostate cancer risk have not been studied previously. We undertook this research to examine the association between dietary patterns and prostate cancer risk using principal components analysis to measure intake of dietary patterns. Specifically, we sought to (1) confirm the presence of the “western” and “prudent” dietary patterns in a nationally representative sample of men, (2) test the hypothesis that a “western” diet is associated with prostate cancer risk, (3) determine if dietary pattern associations with prostate cancer are stronger than those found for more conventional measures of dietary intake, such as total fat, saturated fat, and red meat intake, and (4) examine the extent to which the difference in prostate cancer risk between black and white men in the US can be attributed to interethnic differences in dietary pattern intake. Below, we describe our work towards the tasks outlined in our Statement of Work, as well as the results of additional analyses focusing on dairy, calcium, and vitamin D intake.

BODY

Task 1. Acquisition and setup of NHEFS data (months 1-5)

As described in our progress report, we obtained relevant subsets of NHEFS data from Dr. Rosalind Breslow (Centers for Disease Control), and from Dr. Regina Ziegler (National Cancer Institute) at no cost.

Task 2. Identification of dietary patterns (months 6-12)

a. Perform principal components analyses to identify dietary patterns

As described previously, we used principal components analysis (PCA) on frequency responses to the NHEFS 1982-84 dietary questionnaire to identify patterns of food intake. Three dietary patterns emerged consistently across the split samples (Table 1): (1) a “vegetable-fruit” pattern with high loadings for vegetables, fruits, and seafood (fish and shellfish); (2) a “red meat-starch” pattern with high loadings for red meats, potatoes, salty snacks, cheese, and sweets and desserts; and (3) a “southern” pattern with high loadings for beans, rice, and such traditionally southern foods as cornbread, grits, sweet potatoes, and okra. The same three patterns emerged when we conducted the analysis in black men only.

b. Conduct sensitivity analyses to confirm robustness of results

As described previously, when we repeated analyses collapsing the 105 food items into 37 predefined food groups (1), only two patterns resembling the vegetable-fruit and red meat-starch patterns emerged. We chose not to collapse food items for two main reasons. First, creating groups of potentially dissimilar foods may diminish the ability to identify more specific patterns. Second, grouping foods prior to PCA may attenuate or increase the variance of measures of association between dietary patterns and disease (2). Additional sensitivity analyses are described under section (d).

c. Assess reliability and validity of dietary patterns identified

Our assessment of construct validity was described in the previous progress report. Briefly, we examined distributions of selected sociodemographic and health-related characteristics (3-5) across pattern tertiles (Table 2). We found that associations of the dietary patterns with sociodemographic and health-related characteristics were as expected based on observations of the historical emergence of those patterns (3), confirming the validity of their measurement using PCA.

d. Calculate component scores to represent level of intake of each dietary pattern for each subject

As described previously, we calculated component scores to quantify each individual's level of intake for each pattern by taking the unweighted sum of standardized frequencies of intake for each food associated with the pattern. These scores were used to examine associations of dietary patterns with prostate cancer risk.

Task 3. Examination of dietary pattern – prostate cancer risk associations (months 13-18)

a. Conduct statistical analyses to quantify associations between dietary patterns and prostate cancer risk

Results from our examination of dietary pattern – prostate cancer associations were described in our previous progress report. Briefly, we found that in Cox proportional hazards models (Table 3), prostate cancer risk was not associated with the vegetable-fruit or red meat-starch pattern, but higher intake of the southern pattern showed a reduction in risk (3rd vs. 1st tertile relative risk = 0.6, 95% confidence interval: 0.4, 1.1; trend $p = 0.08$) that approached statistical significance. The inverse association was observed in black and non-black men. A southern dietary pattern may reflect a history of living in the South and serve as an integrative marker of sunlight exposure and protection through 1,25 hydroxyvitamin D production.

b. Perform sensitivity analyses

Risk estimates were not materially different when we excluded 14 prostate cancer cases diagnosed within a year of the dietary interview, re-classified 47 “probable” cases as non-cases, used age rather than time-on-study as the time scale, or excluded cases identified after 1986, when the US Food and Drug Administration approved the prostate-specific antigen (PSA) test for monitoring prostate cancer progression.

c. Quantify associations between single nutrients/foods and prostate cancer risk for comparison with dietary pattern findings

We explored possible explanations for the inverse association for the southern pattern by examining each of the foods associated with it, but none were associated with prostate cancer risk.

Much of our work over the past year has been in pursuing our serendipitous finding that dairy and calcium are associated with prostate cancer risk in this sample. Our finding is consistent with other previous work (6-10). In this

analysis, calcium intake was estimated by multiplying reported frequency of intake of each food in the 1982-4 dietary interview by portion-specific nutrient content estimated from sex- and age-specific 24-hour recall data from the second National Health and Nutrition Examination Survey. We used the same procedures to assign sex- and age-specific vitamin D content per portion size to food items. Values of IU vitamin D per 100 g of food were drawn from the current US Department of Agriculture (USDA) nutrient database (11), supplemented with other published values (12). For mixed dishes, vitamin D-containing ingredients were identified based on recipes available from the USDA Survey Nutrient Database for the 1994-96 Continuing Survey of Food Intakes by Individuals (13) and other recipe sources (14, 15) in order to estimate the amount of vitamin D in the entire mixed dish.

In Cox proportional hazards models (table 4), dairy food intake (3rd vs. 1st tertile RR = 2.2; 95 percent CI: 1.3, 4.0; trend $p = 0.003$) was strongly associated with prostate cancer risk. When each dairy food was examined individually, the increase in risk was observed for low fat milk (3rd vs. 1st tertile RR = 1.6; 95 percent CI: 1.2, 2.1; trend $p = 0.004$) but not for whole milk. Calcium intake was also strongly associated with risk (3rd vs. 1st tertile RR = 2.4; 95 percent CI: 1.5, 3.9; trend $p = 0.0005$). In models for dairy foods that were additionally adjusted for calcium intake, associations for overall dairy (3rd vs. 1st tertile RR = 1.3; 95 percent CI: 0.6, 2.9; trend $p = 0.45$) and low fat milk (3rd vs. 1st tertile RR = 1.1; 95 percent CI: 0.7, 1.6; trend $p = 0.71$) were attenuated, while RR estimates and trend p -values for calcium were not meaningfully changed (table 4). In addition, when we looked at calcium from low fat milk, whole milk, and other food sources, only calcium from low fat milk was associated with risk (3rd vs. 1st tertile RR = 1.8; 95 percent CI: 1.2, 2.6; trend $p = 0.004$). We also saw no association for use of calcium supplements (RR = 0.9; 95 percent CI: 0.3, 2.9), but we identified only 88 men as calcium supplement users. Multivitamins were not included as calcium supplements because of their generally lower calcium content, but use of multivitamins was not associated with risk in these data (RR = 0.9; 95 percent CI: 0.6, 1.4).

Phosphorous was not associated with risk of prostate cancer when calcium was also considered (3rd vs. 1st tertile RR = 0.9; 95 percent CI: 0.5, 1.6; trend $p = 0.82$), nor did we see evidence for an interaction between phosphorous and calcium intake ($p=0.45$). In contrast, with adjustment for calcium intake, vitamin D was inversely associated with prostate cancer risk (3rd vs. 1st tertile RR = 0.5; 95 percent CI: 0.3, 1.0; trend $p = 0.05$). The association for vitamin D was not clearly attributable to any single food or food group when we looked at vitamin D from low fat milk, whole milk, or other foods such as fish or shellfish. Current use of cod liver oil was also not associated with prostate cancer risk (RR = 0.9; 95 percent CI: 0.2, 4.0), but, as in the case for calcium supplements, only a small number of men (N=50) reported its use.

When we examined relative risks for individuals cross-classified according to both calcium and vitamin D intake, risk was elevated primarily in men with high intake of both calcium and vitamin D. Notably, men in this category had

especially high intake of lowfat milk (median 7 servings/week, vs. ≤ 2 in other categories), but not of whole milk or other dairy foods.

Our findings are consistent with the hypothesis that dairy intake increases risk of prostate cancer, possibly through its calcium content, while vitamin D is protective. Reasons for the finding that elevated risk was associated specifically with low fat milk, however, are unclear. Given the implications of these findings with respect to current recommendations regarding both calcium intake and consumption of low fat milk, the mechanisms by which calcium might increase risk should be clarified and confirmed to verify that calcium is indeed the risk factor of interest.

- d. Evaluate dietary patterns as mediator of higher prostate cancer risk in African American vs. white men in NHEFS cohort

Dietary patterns were not pursued as a mediator of the higher prostate cancer risk in African American men because black men remained at higher risk for prostate cancer despite their higher intake of an apparently protective southern pattern. Dairy/calcium intake were not pursued as mediators because African American men did not consume higher amounts of these dietary factors than white men.

Task 4. Final analyses, report writing, and preparation of manuscripts (months 19-24)

A manuscript describing dietary pattern results has been submitted to the journal *Cancer Epidemiology, Biomarkers & Prevention*. A manuscript describing dairy/calcium/vitamin D results has been completed and is being reviewed by co-authors.

Table 1. Factor loadings for foods associated with each dietary pattern, in split samples.

Vegetable-fruit			Red meat-starch		Southern		
sample 1 ^a	sample 2 ^b		sample 1	sample 2	sample 1	sample 2	
Carrots	44	Salty snacks ^c	47	35	Cornbread or hush puppies	60	
Iceberg/head lettuce	47	Fried potatoes	44	39	Okra	51	
Broccoli	49	Pork ^d	42	22	Sweet potatoes or yellow yams	48	
Cauliflower	47	Mixed dishes with meat or cheese	42	35	Quickbread ^g	47	
Leaf lettuce	38	Pickles or olives	41	34	Grits	40	
Salad dressing	40	Chocolate	41	38	Bacon	40	
Grapefruit	32	Ketchup or tomato chili sauce			Beans	36	
Cucumber	39	Beef	37	31	Rice	32	
Green pepper	40	Processed meat ^e	37	40	Watermelon	32	
Summer squash	37	White potatoes	36	34	Liver	29	
Pear	30	Sweets and desserts ^f	35	46		32	
Fresh tomato	36	Cheese sauce, white sauce, thick gravy	34	42			
Fish (fresh or frozen)	33	Corn	34	32			
Brussels sprouts	38	Pasta	30	36			
Apples	32	Ice cream	27	28			
Oranges	37	Cheese and cheese dishes	24	34			
Winter squash	35	Peanuts					
Apricots	24		24	26			
Bananas	33		22	22			
Vegetable soup	32						
Cottage cheese	25						
Strawberries	31						
Canned fish	28						
Cooked tomatoes	26						
Plums	25						
Shellfish	24						
Nuts (not peanuts)	23						
Sweet red pepper	22						
% variance	22		3.3	2.9	2.3	3.4	
Coefficient alpha	5.2		0.64	0.63	0.62	0.65	

^a N=1,866 men^b N=1,913 men^c Includes potato chips, pretzels, crackers, and salted nuts^d Includes roast pork, pork chops, fresh ham, and spare ribs^e Includes sandwich or packaged luncheon meats, hot dogs, and meat spreads^f Includes cakes, donuts, cookies, pies, and candy^g Includes muffins, biscuits, and flour tortillas

TABLE 2. Sociodemographic and health behavior characteristics by dietary pattern tertiles (N=3,544).

	Vegetable-fruit pattern tertiles			Red meat-starch pattern tertiles			Southern pattern tertiles		
	1	2	3	1	2	3	1	2	3
Mean age (y)	57 ± 15	57 ± 15	59 ± 14	61 ± 14	58 ± 14	55 ± 14	57 ± 14	57 ± 14	59 ± 15
Black (%)	14	8	9	16	9	7	3	6	24
Region (%)									
Northeast	25	27	33	31	27	26	35	29	19
Midwest	28	29	24	19	28	33	36	30	14
South	26	21	15	24	22	16	7	11	45
West	21	24	28	26	22	25	22	29	22
Residence (%)									
Rural	44	39	34	33	39	44	33	37	48
Urban	37	35	38	42	36	32	38	36	36
Suburbs	19	26	28	25	25	24	30	27	16
Education (%)									
<HS	47	38	34	43	39	36	32	31	57
HS	32	32	29	26	32	35	34	35	24
>HS	21	30	37	31	29	29	34	34	20
Managerial/professional occupation (%)	18	23	28	26	24	19	25	27	16
Poverty-income ratio (%)*									
≤1	15	8	8	14	9	8	6	7	18
>1-3.5	60	60	53	53	57	63	57	57	60
>3.5	23	32	38	33	34	29	37	36	22
Current smoker (%)	36	31	23	27	29	35	28	28	34
Current multivitamin use (%)	20	23	27	26	24	21	25	25	20
Exercise (%)									
Little/none	37	24	26	33	29	27	29	28	31
Moderate	47	56	49	50	52	50	52	51	48
Much	16	20	24	18	19	24	19	20	21

* Ratio of family income to a Census Bureau-determined poverty threshold for household size and adult/child composition of family; a ratio <1 is considered to represent below poverty level. (N=2,491)

TABLE 3. Relative risk (RR) estimates and 95% confidence intervals (CI) by dietary pattern intake (N=3,616).

Dietary pattern	Prostate cancer cases	Minimal model ^a	Full model ^b
Vegetable-fruit			
tertile 1	35	1.0	1.0
tertile 2	51	1.4 (0.9-1.8)	1.5 (0.9-2.3)
tertile 3	45	1.2 (0.7-1.8)	1.2 (0.7-2.0)
p for trend ^c		0.72	0.64
Red meat-starch			
tertile 1	61	1.0	1.0
tertile 2	38	0.8 (0.5-1.2)	0.7 (0.5-1.2)
tertile 3	32	0.9 (0.6-1.3)	0.8 (0.4-1.4)
p for trend		0.47	0.37
Southern			
tertile 1	45	1.0	1.0
tertile 2	43	0.9 (0.6-1.3)	0.9 (0.6-1.4)
tertile 3	43	0.7 (0.4-1.0)	0.6 (0.4-1.1)
p for trend		0.06	0.08

^a Models adjusted for age, race, and design variables.

^b Models adjusted for age, race, design variables, region, urban/rural residence, education, recreational sun exposure, smoking status, leisure physical activity level, energy intake (tertiles), and alcohol intake.

^c p-value for trend was obtained for each pattern by including in the model a variable representing the median value for each tertile.

TABLE 4. Adjusted* relative risk (RR) estimates and 95% confidence intervals (CI) by tertile of dairy food, calcium, and vitamin D intake for 3,779 adult male participants in the National Health Examination Follow-up Study followed 1982-84 to 1992.

	# cases	Person-years	Adjusted RR (95% CI)	RR (95% CI) additionally adjusted for calcium
Median svgs/wk				
Dairy				
tertile 1	32	9,645	1.0	1.0
tertile 2	40	9,924	1.2 (0.7, 2.1)	1.0 (0.5, 1.9)
tertile 3	64	9,139	2.2 (1.3, 4.0)	1.3 (0.6, 2.9)
p for trend [†]			0.003	0.45
Low fat milk				
tertile 1	60	13,658	1.0	1.0
tertile 2	16	5,527	0.9 (0.5, 1.6)	1.0 (0.6, 1.7)
tertile 3	60	9,522	1.6 (1.2, 2.1)	1.1 (0.7, 1.6)
p for trend			0.004	0.71
Whole milk				
tertile 1	71	13,470	1.0	1.0
tertile 2	24	6,004	0.9 (0.6, 1.5)	1.2 (0.7, 1.9)
tertile 3	41	9,234	0.8 (0.5, 1.2)	0.7 (0.5, 1.1)
p for trend			0.19	0.12

TABLE 4 (continued).

	# cases	Person-years	Adjusted RR (95% CI)	RR (95% CI) additionally adjusted for calcium
mg total calcium/day				
Calcium				
tertile 1	28	9,729	1.0	--
tertile 2	40	9,596	1.2 (0.7, 1.9)	
tertile 3	68	9,382	2.4 (1.5, 3.9)	
p for trend			0.0005	
Calcium from low fat milk				
tertile 1	32	9,610	1.0	--
tertile 2	45	9,475	1.3 (0.7, 2.2)	
tertile 3	59	9,623	1.8 (1.2, 2.6)	
p for trend			0.004	
Calcium from all other sources				
tertile 1	37	9,734	1.0	--
tertile 2	52	9,674	1.1 (0.7, 1.7)	
tertile 3	47	9,300	1.0 (0.6, 1.5)	
p for trend			0.78	
IU vitamin D/day				
Vitamin D				
tertile 1	36	9,701	1.0	1.0
tertile 2	42	9,525	0.9 (0.6, 1.3)	0.6 (0.4, 1.0)
tertile 3	58	9,481	1.3 (0.9, 2.0)	0.5 (0.3, 1.0)
p for trend			0.18	0.05

* Models adjusted for age, race (white, black, other race), and design variables (dichotomized age (< 65 vs. ≥ 65 years), poverty census enumeration district (residence vs. non-residence), and family income (< \$3,000, \$3,000-\$6,999, \$7,000-\$9,999, \$10,000-\$14,999, and ≥ \$15,000)).

† p-value for trend was obtained for each pattern by including in the model a variable representing the median value for each tertile.

KEY RESEARCH ACCOMPLISHMENTS

- successfully conducted planned analyses towards research objectives – namely:
 - in a nationally representative sample of men, confirmed the presence of the two dietary patterns expected *a priori*, and identified a new dietary pattern in the sample
 - examined dietary patterns in relation to prostate cancer risk, finding no association for the red meat-starch pattern as was originally expected, but finding an inverse association for the southern pattern
 - found stronger associations for the southern pattern than for any single food in the southern pattern
- successfully pursued a serendipitous finding of higher risk associated with dairy and calcium intake, with the following findings:
 - in a nationally representative sample of men, intake of dairy foods and calcium was associated with strong increased risk for prostate cancer
 - elevated risk observed for dairy foods was seen only for low fat milk and not for any other dairy items
 - vitamin D intake was inversely associated with prostate cancer risk – an effect not attributable to any specific vitamin D-rich foods, but evident only when all dietary sources were considered together

REPORTABLE OUTCOMES

Manuscripts

1. Tseng M, Breslow R, DeVellis RF, Ziegler R. Dietary patterns and prostate cancer in the NHANES I Epidemiologic Followup Study Cohort. *Submitted manuscript*.
2. Tseng M, Breslow R, Ziegler R. Dairy, calcium, and vitamin D intake and prostate cancer risk in the NHEFS Cohort. *Manuscript in preparation*.

Abstracts

1. Tseng M, Breslow R, Babb J, DeVellis RF, Ziegler R. Dietary patterns and prostate cancer in the NHANES I Epidemiologic Followup Study Cohort (abstr). *Proc Am Assoc Cancer Res* 43: 933, 2002.
2. Tseng M, Breslow R, Babb J, DeVellis RF, Ziegler R. Dietary patterns and prostate cancer in the NHANES I Epidemiologic Followup Study Cohort (abstr). *Am J Epidemiol* 155: S55, 2002.
3. M Tseng, R Breslow, J Babb, RF DeVellis, R Ziegler. Dairy, Calcium, and Prostate Cancer in the NHANES I Epidemiologic Followup Study (abstr). *Am J Epidemiol* 155: S55, 2002.

Presentations

1. Tseng M, Breslow R, Babb J, DeVellis RF, Ziegler R. (2002). Dietary patterns and prostate cancer in the NHANES I Epidemiologic Followup Study Cohort. Presented as poster at the American Association for Cancer Research meeting, San Francisco, CA, and at the Society for Epidemiologic Research meeting, Palm Desert, CA.

2. M Tseng, R Breslow, J Babb, RF DeVellis, R Ziegler. (2002). Dairy, Calcium, and Prostate Cancer in the NHANES I Epidemiologic Followup Study. Presented at the Society for Epidemiologic Research meeting, Palm Desert, CA.

CONCLUSIONS

We found that prostate cancer risk was not clearly associated with either the red meat-starch or the vegetable-fruit pattern, but we observed a suggestive, inverse association for the southern pattern. The association was observed in both black and non-black men and was not attributable to any individual foods within the pattern or to any nutrients of prior interest. A southern dietary pattern may reflect a history of living in the South and serve as an integrative marker of sunlight exposure and protection through 1,25 hydroxyvitamin D production. However, better characterization of the pattern would offer more information on potentially beneficial features of the diet or of its associated lifestyle. Thus, our findings should be explored and confirmed in other data to clarify interpretation of these observations. While a pattern approach might yield a valuable perspective in diet-disease studies, strategies for improving methods of identifying and evaluating dietary patterns also require further consideration.

Consistent with our hypothesis that a vitamin D-related pathway is protective, we found that prostate cancer risk was elevated with higher intake of dairy foods and calcium, particularly calcium from low fat milk, while risk was inversely associated with intake of vitamin D. Reasons for the finding that elevated risk was associated specifically with low fat milk, however, are unclear. Given the implications of these findings with respect to current recommendations regarding both calcium intake and consumption of low fat milk, the mechanisms by which calcium might increase risk should be clarified and confirmed to verify that calcium is indeed the risk factor of interest.

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LIST OF PERSONNEL

Marilyn Tseng, Ph.D., Principal Investigator
James Babb, Ph.D., Biostatistician

APPENDICES

Tseng M, Breslow R, Babb J, DeVellis RF, Ziegler R. Dietary patterns and prostate cancer in the NHANES I Epidemiologic Followup Study Cohort. *Submitted manuscript*.

**DIETARY PATTERNS AND PROSTATE CANCER RISK
IN THE NHEFS COHORT**

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Running head: Dietary Patterns and Prostate Cancer

ABSTRACT

Ecologic studies implicate a “western” diet in prostate cancer development, but whether dietary patterns measured in individuals are associated with risk has not been studied previously. We examined this issue using prospective data from the nationally representative US Health Examination Epidemiologic Follow-up Study. Among 3,779 men followed from 1982-4 to 1992, 136 incident cases were identified. Using principal components analysis on responses to a 105-item dietary questionnaire, three distinct patterns were identified: a vegetable-fruit pattern, a red meat-starch pattern characterized by red meats, potatoes, cheese, salty snacks, and desserts, and a southern pattern characterized by such foods as cornbread, grits, sweet potatoes, okra, beans, and rice. In adjusted proportional hazards models, prostate cancer risk was not associated with the vegetable-fruit or red meat-starch pattern, but higher intake of the southern pattern showed a reduction in risk (3rd vs. 1st tertile relative risk = 0.6, 95% confidence interval: 0.4, 1.1; trend $p = 0.08$) that approached statistical significance. The inverse association was observed in black and non-black men and was not attributable to intake of any individual foods or nutrients. A southern dietary pattern may reflect a history of living in the South and serve as an integrative marker of sunlight exposure and protection through 1,25 hydroxyvitamin D production. Further evaluation and better characterization of the pattern would offer more information on potentially beneficial features of the diet or its associated lifestyle.

INTRODUCTION

In 2003, prostate cancer is expected to remain the most commonly diagnosed cancer and the second leading cause of cancer death in US men (1). Although risk factors for prostate cancer have been identified, only age, ethnicity, and family history of prostate cancer are well-established (1). Thus, feasible measures for primary prevention of the disease remain limited.

Epidemiologic and laboratory research suggest that dietary intake is one factor that might be modified to reduce risk (2, 3). In particular, ecologic (4-6) and migrant (7) studies have implicated a "western" dietary pattern as a risk factor for prostate cancer. Whether dietary patterns measured at the level of the individual are associated with prostate cancer risk has not been studied previously, in part because of the relative novelty of the approach but also because standard methods for identifying, measuring, and interpreting dietary patterns are only now being developed. By examining exposure to several related dietary factors simultaneously, quantifying the aggregate risk associated with a particular combination of foods, and offering results that are based on actual dietary practice and more easily translated into useful recommendations, a dietary pattern approach provides a useful complement to findings based on single nutrients or single food groups.

In research using principal components analysis (PCA) to identify and quantify dietary patterns, two patterns emerge fairly consistently in US samples: one characterized by intake of vegetables and fruits, and a western-style pattern based on red meat and starch (8-10). The western pattern has been related to increased risk of colon cancer (8, 11), cardiovascular disease (12), and diabetes (13). The objectives of our analyses were to identify dietary patterns in a nationally representative sample of US men using PCA and to examine for the first time their

associations with prostate cancer risk in prospectively collected data, with the goal of clarifying the importance of specific dietary patterns to the development of prostate cancer.

MATERIALS AND METHODS

Study population

The study sample included male participants in the first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study (NHEFS). NHANES I, conducted between 1971 and 1975, used a multistage sampling design to obtain a national probability sample of the noninstitutionalized civilian population of the United States, excluding Alaska, Hawaii, and Native American reservation lands (14, 15). The elderly and persons residing in poverty areas were oversampled. About 70 percent of those sampled were both interviewed and medically examined in NHANES I.

NHEFS was a longitudinal study of the 14,407 participants between the ages of 25 and 74 years at the time of the initial survey (16-19). Participants were followed for health and vital status through 1992. At interviews conducted in 1982-84, 1986, 1987, and 1992, participants or their proxies were interviewed. Also, health records were obtained for instances in which participants reported an overnight stay in a health care facility between the baseline examination and last follow-up visit. Death certificates were obtained for deaths during the follow-up period and were identified by the National Death Index or other tracing mechanisms. Health records were obtained for over 70 percent of reported overnight stays and death certificates were obtained for 99 percent of deaths occurring between 1971-75 and the 1992 follow-up (19).

Because food frequency data obtained in the 1971-75 interview included questions on only 13 broad food categories, we used more detailed data from a 105-item food frequency

questionnaire administered in 1982-84. Thus, 1982-84 served as the baseline for these analyses. Of the 14,407 NHEFS participants, 5,811 were men. Of these, 1,202 died prior to the 1982-84 interview, 351 could not be traced, and 333 were not interviewed in 1982-84. Subjects were further excluded from the remaining study sample if they had a diagnosis of prostate cancer at or before the 1982-84 interview ($n = 57$), did not complete the diet questionnaire ($n = 79$), or had energy intake of < 500 or $> 4,400$ kcal/day ($n = 10$), leaving 3,779 men available for analysis.

Identification of prostate cancer cases

Cases of invasive prostate cancer were identified following a procedure described by Breslow et al. (20). Briefly, potential cases were all men with an International Classification of Diseases, Ninth Revision, Clinical Modification code of 185 (invasive prostate cancer), 233.4 (prostate carcinoma in situ), v 10.46 (personal history of malignant prostate neoplasm), or 60.3-60.5 (prostatectomy surgical procedures) recorded in at least one of the following sources of data: (1) a first diagnosis of prostate cancer reported at any of the follow-up interviews conducted in 1986, 1987, or 1992; (2) one or more hospital stays during the follow-up period with a discharge diagnosis coded as any of the codes given above; (3) a death certificate with underlying or nonunderlying cause of death coded as any of the codes given above. Archived records of interviews and overnight health care facility stays were then reviewed. "Definite" case status was assigned if it could be confirmed from histopathology reports or medical records. Determinations based only on interview or death certificate data were assigned "probable" case status, although self-reported cases were unconfirmed by hospital records in some instances because of lack of response from some hospitals. Of 136 cases diagnosed during the follow-up

of the 3,779 men from the 1982-84 interview, 89 were considered “definite” cases, and an additional 47 were considered “probable” cases.

Data collection

Information on dietary intake was obtained from a 105-item food frequency questionnaire administered in the 1982-84 interview. The questionnaire was designed to include foods commonly consumed in the US diet and covered the major food groups, including meats, fish, poultry, grains, fruits, vegetables, dairy products, sweets, snacks, and beverages. Intake of specific nutrients such as energy, total fat, and vitamin A was estimated by multiplying frequency of intake of each food by the nutrient content for the food’s portion size. Because the 1982-84 NHEFS dietary interview collected only frequency information, information on nutrient content and portion size for each food was based on sex- and age-specific 24-hour recall data from the second National Health and Nutrition Examination Survey (NHANES II), a separate national survey conducted in 1976-80. A detailed description of the method used to assign nutrient content and portion size to each food item in the NHEFS dietary questionnaire using NHANES II data has been published (21).

Other information available from the 1982-84 interview included race, place of residence, longest held occupation, family income, first-degree family history of prostate cancer, current weight, alcohol intake, smoking behavior, sun exposure, level of physical activity, and current multivitamin use. Information on height and level of education was available from the 1971-75 interview.

Identification of dietary patterns

Patterns of food intake were identified by PCA (22, 23) using frequency responses to the dietary questionnaire. (An example of SAS programming statements used to run the analysis is provided at <http://www.fccc.edu/research/labs/tseng/TsengDOD01.html>.) Individuals were randomly placed into one of two equally sized groups, or split-samples. For the first split-sample, a matrix of correlations among frequency of consumption for the questionnaire food items was constructed and entered in the PCA. Extraction of principal components was followed by orthogonal rotation of retained components to allow for interpretability (22, 23). The number of components to retain for rotation was based on examination of scree plots and interpretability of the components (23); although another common strategy is to rotate all factors with eigenvalues greater than 1.0, this method has been shown to overestimate the number of components (23). The analysis was repeated in the second split-sample in order to confirm reproducibility of patterns identified. Cronbach's coefficient alpha (24) was used to evaluate internal consistency for each component retained. In psychometric research, a coefficient alpha of ≥ 0.70 generally indicates acceptable reliability (25), although in previous research, dietary pattern scales with coefficient alphas as low as 0.5-0.6 were predictive of disease (26). As an additional assessment of the robustness of the patterns identified, we used oblique rather than orthogonal rotation, but the same patterns emerged.

A component score was calculated for each dietary pattern for each individual to represent the individual's level of intake for the pattern. The score for each pattern was computed as a linear composite of the foods with meaningful loadings ($\geq |0.20|$) for only that pattern. Scores were calculated by taking the unweighted sum of standardized frequencies of intake for each food associated with the pattern. When we computed pattern scores as a linear composite of all

variables weighted based on regression results (27), scores calculated the two different ways were highly correlated ($r > 0.85$), and estimates of relative risk (RR) for prostate cancer were similar.

We examined construct validity of the patterns, or the extent to which they behave as expected theoretically with respect to other variables (28), by describing their associations with sociodemographic and lifestyle variables among 3,544 men with complete variable data. The variables, selected based on social and historical descriptions of the development of those patterns (29-31), included age, place of residence (rural, urban, suburban), socioeconomic status (SES), and various health-related behaviors.

Data analysis

Follow-up time was calculated by subtracting the 1982-84 interview date from last date known to be alive and free of prostate cancer (date of last interview, contact, or death) for non-cases, or from date of prostate cancer diagnosis for cases. For four cases identified from death certificate data only, the 1982-84 interview date was subtracted from date of death rather than from date of diagnosis.

Adjusted RR of prostate cancer was estimated for tertiles of pattern scores using Cox proportional hazards models while adjusting for age (continuous years) and race (white, black, or other race). Other variables – including US region, urban/rural residence, education, first-degree family history of prostate cancer, current body mass index, recreational physical activity, recreational and occupational sun exposure, multivitamin use, smoking status, and past and current alcohol consumption – were evaluated as confounders based on their associations with predictor and response variables, and by comparing unadjusted and adjusted estimates from

regression analyses. Final multivariate models included 3,616 men with complete covariate data and adjusted for age, race, US region (Northeast, Midwest, South, West), residence (rural, urban, suburban), education (< high school, high school completion, > high school), recreational sun exposure (little, occasional, frequent), recreational physical activity (little/none, moderate, much), smoking status (never, former, current), current alcohol intake (none, little, moderate, heavy), and energy intake (tertiles). All covariates were coded using dummy variables to allow for non-linear associations across categories. Controlling for energy as a continuous variable produced no meaningful changes in estimates.

P-values for linear trend were obtained for each dietary pattern by including an ordinal variable representing the scaled median value for each tertile in the multivariate model controlling for the covariates listed above. To examine the possibility of effect modification by race, we ran proportional hazards models in black and non-black men separately; men of ethnicities other than white or black were too few ($n = 46$) to allow for separate analysis. Because of the small number of black cases ($n = 27$), we dichotomized pattern scores for all men at the median value for black men. P-values for interaction were obtained from a model including all men, with a pattern category x race interaction term.

In multivariate models controlling for the same covariates, we also examined the effects of specific foods and nutrients potentially related to risk of prostate cancer, including red meat, dairy, fruits and vegetables, tomatoes, energy, total and saturated fat, calcium, vitamin A, and dietary fiber (32-35). Nutrient values were log-transformed as necessary and energy-adjusted using the residual method (36). RRs were estimated for tertiles of intake relative to the lowest tertile, but for infrequently consumed items such as okra and grits, estimates were for consumption vs. non-consumption. To account for sample weighting from the survey design, all

final models also included the following design variables: age (< 65 vs. \geq 65 years), poverty census enumeration district (residence vs. non-residence), and family income (< \$3,000, \$3,000-\$6,999, \$7,000-\$9,999, \$10,000-\$14,999, and \geq \$15,000) (37), although results from models with and without design variables were similar.

RESULTS

Mean age of the men in the study sample was 58 years, 11 percent were African-American, and their usual residence was roughly equally distributed among the four regions of the US. Over a mean follow-up of 7.6 years (range <1-10.7 years), 136 prostate cancer cases were identified in the cohort of 3,779 men.

In PCA, three dietary patterns emerged consistently across the split samples (table 1): (1) a “vegetable-fruit” pattern with high loadings for vegetables, fruits, fish, and shellfish; (2) a “red meat-starch” pattern with high loadings for red meats, potatoes, salty snacks, cheese, and sweets and desserts; and (3) a “southern” pattern with high loadings for beans, rice, and such traditionally southern US foods as cornbread, grits, sweet potatoes, and okra. The same three patterns emerged when we conducted the analysis in black men only (results not shown). Thus, calculation of pattern scores was based on the PCA solution including all men.

As an assessment of construct validity, we described the distributions of selected sociodemographic and health-related characteristics across pattern tertiles (table 2). Men with high intake of the vegetable-fruit pattern were more likely to be white and of higher SES, to live in the northeastern and western US and in suburbs, and to use multivitamins, exercise, and not smoke. Men with high intake of the red meat-starch pattern were more likely to be white and younger in age, to live in rural areas and in the Midwest, and to smoke, exercise, and not use

multivitamins. Associations of the red meat-starch pattern with SES indicators reflected neither especially high nor especially low SES: men with high intake were more likely to have graduated high school but not college and were more likely to be above the poverty level but not at the highest incomes. In contrast, men with high intake of the southern pattern were more likely to be black, to be of lower SES, to live in rural areas and in the South, and to smoke and not use multivitamins.

In Cox proportional hazards models (table 3), while the red meat-starch pattern was not associated with prostate cancer, intermediate intake of the vegetable-fruit pattern showed a slight elevation of risk (RR = 1.5; 95 percent confidence interval (CI): 0.9, 2.3). However, for neither pattern was there evidence of a trend, and none of the point estimates reached statistical significance. Higher intake of the southern pattern showed a trend ($p=0.08$) and a reduction in risk in the third tertile (3rd vs. 1st tertile RR = 0.6; 95 percent CI: 0.4, 1.1) that approached statistical significance. Risk estimates were not materially different when we excluded 14 prostate cancer cases diagnosed within a year of the dietary interview, re-classified 47 “probable” cases as non-cases, conducted analyses using SUDAAN (38), or used age rather than time-on-study as the time scale (39). In race-specific analyses, the association between the southern dietary pattern and prostate cancer risk was more pronounced in black men (above vs. below median RR = 0.2; 95 percent CI: 0.2, 0.6), but estimates were based on a small number of cases, and the p -value for interaction was not significant.

We explored possible explanations for the inverse association for the southern pattern by examining each of the foods associated with it, but none were associated with prostate cancer risk (results not shown). Dietary patterns were also correlated with intake of other specific foods and nutrients that have previously been linked to prostate cancer risk (table 2), but with the

exception of dairy foods and calcium (described in a separate manuscript), none of these were clearly associated with disease in our data; RR estimates were all around one and showed no trend in either direction (results not shown). However, men with an intermediate level of fruit intake had a non-significantly elevated risk (2nd vs. 1st tertile RR = 1.3; 95 percent CI: 0.8, 2.1).

Since 1986, when the US Food and Drug Administration approved the prostate-specific antigen test for monitoring prostate cancer progression, incidence has increased more steeply in men of higher SES and, presumably, with better awareness of or access to screening modalities (40). To explore the possibility of detection bias, we conducted additional analyses including only cases identified before 1986. The inverse association for the southern pattern persisted (3rd vs. 1st tertile RR = 0.4; 95 percent CI: 0.2, 0.9), but estimates were based on only 46 cases.

DISCUSSION

In a nationally representative sample of men, we identified three dietary patterns: a vegetable-fruit pattern, a red meat-starch pattern, and a southern pattern. The red meat-starch pattern was not associated with disease, but intermediate intake of the vegetable-fruit pattern was non-significantly associated with increased prostate cancer risk. Intake of the southern pattern showed a trend that was suggestive of an inverse association and that could not be attributed to any specific foods within the pattern.

Identification of the vegetable-fruit and western patterns in this sample is consistent with findings of previous US studies (8-10) and with anthropological and historical accounts of traditional American eating habits (29-31). Moreover, their associations with sociodemographic and health-related characteristics were as expected based on observations of the historical emergence of those patterns (29), confirming the validity of their measurement using PCA (28,

41). Although other studies have identified patterns specific to Mexican Americans (26, 42), ours is the first, to our knowledge, to identify a southern US pattern in a sample not limited to a specific ethnic or regional group. Our results further suggest that the pattern is not a spurious finding: The pattern emerged across split samples in our analyses, was easily recognizable as a distinct pattern, and its associations with sociodemographic characteristics were consistent with social/cultural descriptions of the pattern (31), supporting the pattern's construct validity.

We surmise that we were able to identify the southern pattern because the food frequency questionnaire included such specifically southern items as cornbread, grits, and okra, and because we did not group the 105 food items from the questionnaire for the analysis. We chose not to collapse food items for several reasons. First, creating groups of potentially dissimilar foods may diminish the ability to identify more specific patterns. Indeed, when we collapsed foods into 35 predefined food groups (9), only two rather than three patterns clearly emerged – the vegetable-fruit and red meat-starch patterns (results not shown). Ability to identify dietary patterns, therefore, is strongly dependent both on the food items included in the instrument and on how foods are aggregated into groups for analysis. That the southern pattern was reproducible across split-samples and was associated with other variables as theoretically expected suggests that its identification in our data was not a spurious finding; rather, collapsing foods into groups might have prevented finding a true pattern.

Grouping foods prior to PCA may also attenuate or increase the variance of measures of association between dietary patterns and disease (43). Collapsing foods into groups would likely have produced patterns that explained more of the total variation in food intake than the 11% explained by the three patterns in our study. However, the primary objective of performing PCA in diet-disease studies is not to explain total variation, but to examine associations of

conceptually meaningful patterns with disease risk. Indeed, McCann et al. (43) have demonstrated that increasing the amount of variance explained by collapsing foods into groups does not improve estimates of disease risk.

Factors that might have obscured or biased associations in our study merit discussion. Using PCA to quantify dietary patterns may involve some measurement error, for example. However, reasonably high (> 0.60) coefficient alphas for the three patterns indicate good internal reproducibility for each pattern, and using an alternative method to calculate pattern scores (27) produced similar associations with risk. Although prostate-specific antigen testing was relatively uncommon before 1991 (44), some bias in detecting prostate cancer cases remains possible as well, given the associations of dietary patterns with urban/rural residence and SES. RR estimates were largely unchanged when we controlled for sociodemographic factors that may be linked to screening such as education (40), and when we limited cases to those identified before government approval of prostate-specific antigen testing in 1986. However, information on access to screening and screening behavior was not available to evaluate this possibility more directly.

We found a slightly elevated prostate cancer risk with intermediate intake of the vegetable-fruit pattern but no clear trend. When we examined fruits and vegetables separately, we observed no association for vegetables, but a slightly elevated risk for an intermediate level of fruit intake. Our finding is similar to that of other studies that observed a positive association with fruit intake (32), but the explanations for this finding are not known. We observed no elevation in risk for selected nutrients associated with fruit or vegetable intake.

Our results do not support the hypothesis that a western pattern increases risk of prostate cancer. In our sample, red meat-starch pattern intake, intake of red meat as a food group, and

intake of energy, total fat, and saturated fat were not associated with disease, although previous cohort studies have fairly consistently found positive associations for red meat and for saturated and animal fat (34). Besides detection bias, this may also reflect simply the lack of strong influence of overall adult diet on risk, insufficient variability in intake, or inaccurate measurement of the underlying pattern. A clearer understanding of dietary pattern measurement is warranted before more definite conclusions can be drawn. Notably, a western pattern was also not associated with colorectal or breast cancer in recent analyses in the Swedish Mammography cohort (45, 46).

We observed a non-significant but suggestive inverse association for the southern pattern. This finding is especially intriguing because black men were more likely to consume this pattern yet remained at higher risk for prostate cancer. In race-specific analyses, the apparent inverse association persisted in both black and non-black men. The association was not attributable to any individual foods within the pattern or to any nutrients of prior interest. Our finding suggests that prostate cancer incidence might increase with movement away from a traditional southern cuisine. Alternatively, the finding raises additional questions regarding interpretation of dietary pattern measures. For example, a southern dietary pattern may reflect a history of living in the South and serve as an integrative marker of sunlight exposure (47) rather than a simple measure of overall dietary habits. Sunlight has been hypothesized to protect against prostate cancer through 1,25 hydroxyvitamin D production (48), and recent work also offers evidence that both childhood and cumulative, lifetime sun exposure are associated with reduced risk (49). Although we controlled for other lifestyle factors in our analysis (including current residence in the South) and considered several others as potential confounders in preliminary analyses, it remains possible that our measure for the southern pattern represents earlier-life or long-term sunlight

exposure. Our findings emphasize the importance of considering the context of any given dietary pattern in order to understand the relevance of the diet or of its associated lifestyle on health status.

In summary, we found that prostate cancer risk was not clearly associated with either the red meat-starch or the vegetable-fruit pattern, but we observed a suggestive, inverse association for the southern pattern. The association was observed in both black and non-black men and was not attributable to any individual foods within the pattern or to any nutrients of prior interest. A southern dietary pattern may reflect a history of living in the South and serve as an integrative marker of sunlight exposure and protection through 1,25 hydroxyvitamin D production. However, better characterization of the pattern would offer more information on potentially beneficial features of the diet or of its associated lifestyle. Thus, our findings should be explored and confirmed in other data to clarify interpretation of these observations. While a pattern approach might yield a valuable perspective in diet-disease studies, strategies for improving methods of identifying and evaluating dietary patterns also require further consideration.

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² Abbreviations used are: CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; NHEFS, NHANES I Epidemiologic Follow-up Study; PCA, principal components analysis; RR, relative risk; SES, socioeconomic status.

TABLE 1. Factor loadings for foods associated with each dietary pattern, in split samples of 3,779 adult male participants in the National Health Examination Follow-up Study, 1982-84.

	Vegetable-fruit		Red meat-starch		Southern	
	sample 1*	sample 2†	sample 1	sample 2	sample 1	sample 2
Carrots	55	44	Salty snacks §	47	35	Cornbread or hush
Iceberg/head lettuce	49	47	Fried potatoes	44	39	puppies
Broccoli	48	49	Pork ¶	42	22	Okra
Cauliflower	46	47	Mixed dishes with			Sweet potatoes or
Leaf lettuce	45	38	meat or cheese	42	35	yellow yams
Salad dressing	42	40	Pickles or olives	41	34	Quickbread ††
Grapefruit	40	32	Chocolate	41	38	Grits
Cucumber	40	39	Ketchup or tomato			Bacon
Green pepper	40	40	chili sauce	37	31	Beans
Summer squash	38	37	Beef	37	40	Rice
Pear	37	30	Processed meat #	36	34	Watermelon
Fresh tomato	35	36	White potatoes	35	46	Liver
Fish (fresh or frozen)	35	33	Sweets/desserts **	34	42	
Brussels sprouts	35	38	Cheese sauce, white			
Apples	35	32	sauce, thick gravy	34	32	
Oranges	34	37	Corn	30	36	
Winter squash	34	35	Pasta	27	28	
Apricots	33	24	Ice cream	24	34	

TABLE 2 (continued).

	Vegetable-fruit		Red meat-starch		Southern	
	sample 1*	sample 2†	sample 1	sample 2	sample 1	sample 2
Bananas	32	33	Cheese and cheese			
Vegetable soup	32	25	24	26		
Cottage cheese	31	25	22	22		
Strawberries	28	26				
Canned fish	26	28				
Cooked tomatoes	25	24				
Plums	24	24				
Shellfish	23	28				
Nuts (not peanuts)	22	21				
Sweet red pepper	22	22				
% variance	5.2	4.5	3.3	2.9	2.3	3.4
Coefficient alpha	0.77	0.74	0.64	0.63	0.62	0.65

* N=1,866 men

† N=1,913 men

§ Includes potato chips, pretzels, crackers, and salted nuts

¶ Includes roast pork, pork chops, fresh ham, and spare ribs

Includes sandwich or packaged luncheon meats, hot dogs, and meat spreads

** Includes cakes, donuts, cookies, pies, and candy

†† Includes muffins, biscuits, and flour tortillas

TABLE 2. Sociodemographic and health behavior characteristics and intake of selected dietary factors for first and third dietary pattern tertiles in 3,544 adult male participants in the National Health Examination Follow-up Study, 1982-84.

	Vegetable-fruit pattern tertiles			Red meat-starch pattern tertiles			Southern pattern tertiles		
	1	3		1	3		1	3	
Mean (SD) age (y)	57 (15)	59 (14)		61 (14)	55 (14)		57 (14)	59 (15)	
Black (%)	14	9		16	7		3	24	
Region (%)									
Northeast	25	33		31	26		35	19	
Midwest	28	24		19	33		36	14	
South	26	15		24	16		7	45	
West	21	28		26	25		22	22	
Residence (%)									
Rural	44	34		33	44		33	48	
Urban	37	38		42	32		38	36	
Suburbs	19	28		25	24		30	16	
Education (%)									
< high school	47	34		43	36		32	57	
completed high school	32	29		26	35		34	24	
>high school	21	37		31	29		34	20	
Poverty-income ratio (%)*									
≤1	15	8		14	8		6	18	
>1-3.5	60	53		53	63		57	60	
>3.5	23	38		33	29		37	22	

TABLE 2 (continued).

	Vegetable-fruit pattern tertiles			Red meat-starch pattern tertiles			Southern pattern tertiles		
	1	3		1	3		1	3	
Current smoker (%)	36	23		27	35		28	34	
Current multivitamin use (%)	20	27		26	21		25	20	
“Much” exercise (%)	16	24		18	24		19	21	
Median times per week									
Red meat	8.0	8.0		5.1	11.0		7.0	9.0	
Dairy	9.0	11.0		8.0	13.0		10.2	9.5	
Fruits and vegetables	13.9	38.2		21.5	27.0		20.1	29.0	
Tomatoes	3.1	6.0		3.3	6.0		4.3	4.8	
Median per day									
Energy (kcal)	1,665	2,057		1,448	2,329		1,704	2,047	
Total fat (% kcal)	35.2	33.2		31.9	36.3		34.3	34.1	
Saturated fat (% kcal)	12.5	11.3		10.8	12.8		12.1	11.7	
Fiber (g / 1000 kcal)	6.5	9.7		8.8	7.5		7.4	8.5	
Vitamin A (IU / 1000 kcal)	3,272	4,938		4,527	3,643		3,359	4,832	
Vitamin C (mg / 1000 kcal)	50	96		87	66		72	73	
Calcium (mg / 1000 kcal)	338	371		364	348		370	341	

* Ratio of family income to a Census Bureau-determined poverty threshold for household size and adult/child composition of family; a ratio <1 is considered to represent below poverty level. (N=2,491)

TABLE 3. Adjusted relative risk (RR) estimates and 95% confidence intervals (CI) by dietary pattern intake for 3,616 adult male participants in the National Health Examination Follow-up Study followed 1982-84 to 1992.

Dietary pattern	# cases	Person-years	Minimal model*		Full model†	
			RR	95% CI	RR	95% CI
Vegetable-fruit						
tertile 1	35	9,053	1.0		1.0	
tertile 2	51	9,432	1.4	0.9, 1.8	1.5	0.9, 2.3
tertile 3	45	9,359	1.2	0.7, 1.8	1.2	0.7, 2.0
p for trend ‡				0.72		0.64
Red meat-starch						
tertile 1	61	8,823	1.0		1.0	
tertile 2	38	9,431	0.8	0.5, 1.2	0.7	0.5, 1.2
tertile 3	32	9,590	0.9	0.6, 1.3	0.8	0.4, 1.4
p for trend				0.47		0.37
Southern						
tertile 1	45	9,562	1.0		1.0	
tertile 2	43	9,606	0.9	0.6, 1.3	0.9	0.6, 1.4
tertile 3	43	8,675	0.7	0.4, 1.0	0.6	0.4, 1.1
p for trend				0.06		0.08

* Models adjusted for age, race (white, black, other race), and design variables (dichotomized age (< 65 vs. ≥ 65 years), poverty census enumeration district (residence vs. non-residence), and family income (< \$3,000, \$3,000-\$6,999, \$7,000-\$9,999, \$10,000-\$14,999, and ≥ \$15,000)).

† Models adjusted for above variables, and US region (Northeast, Midwest, South, West), residence (rural, urban, suburban), education (< high school, high school completion, > high school), recreational sun exposure (little, occasional, frequent), recreational physical activity (little/none, moderate, much), smoking status (never, former, current), current alcohol intake (none, little, moderate, heavy), and energy intake (tertiles).

‡ p-value for trend was obtained for each pattern by including in the model a variable representing the median value for each tertile.